(19) World Intellectual Property Organization

International Bureau





(43) International Publication Date 4 November 2004 (04.11.2004)

PCT

(10) International Publication Number $WO\ 2004/094605\ A3$

(51) International Patent Classification⁷: 48/00

A61K 38/00,

(21) International Application Number:

PCT/US2004/012066

(22) International Filing Date: 19 April 2004 (19.04.2004)

(25) Filing Language:

English

(26) Publication Language:

English

(30) Priority Data: 60/463,764

17 April 2003 (17.04.2003) US

- (71) Applicant (for all designated States except US): MOUNT SINAI SCHOOL OF MEDICINE OF NEW YORK UNIVERSITY [US/US]; One Gustav L. Levy Place, New York, New York 10029-6574 (US).
- (72) Inventors; and
- (75) Inventors/Applicants (for US only): HORVATH, Curt [US/US]; 254 E. 68th Street, #4C, New York, New York 10021 (US). RODRIGUEZ, Jason [US/US]; New York, NY (US). ULANE, Chrstine [US/US]; 50 East 98th Street, Apt. 14i1, New York, New York 10029 (US). PARISIEN, Jean-Patrick [HT/US]; 85-25 120th Street, Apt. 2A, Kew Gardens, New York 11415 (US).
- (74) Agents: LORENZ, Todd, A. et al.; DORSEY & WHIT-NEY LLP, 4 Embarcadero Center, Suite 3400, San Francisco, California 94111 (US).
- (81) Designated States (unless otherwise indicated, for every kind of national protection available): AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM,

TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW.

(84) Designated States (unless otherwise indicated, for every kind of regional protection available): ARIPO (BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).

Declaration under Rule 4.17:

as to applicant's entitlement to apply for and be granted a patent (Rule 4.17(ii)) for the following designations AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VC, VN, YU, ZA, ZM, ZW, ARIPO patent (BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

Published:

- with international search report
- (88) Date of publication of the international search report: 31 March 2005
- (15) Information about Correction:

Previous Correction:

see PCT Gazette No. 02/2005 of 13 January 2005, Section II

For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

(54) Title: METHODS AND COMPOSITIONS FOR INHIBITING STAT SIGNALING PATHWAYS

(57) Abstract: The invention relates to compositions and methods for modulating cell signaling mediated by signal transducers and activators of transcription (STAT). The compositions target cellular STAT3 and STAT1 protein, particularly STAT3, for degradation via the ubiquitination pathway. Thus, the STAT inhibiting agents are useful for inhibiting STAT mediated signal transduction events, such as responses to IL6 and v-Src, any may be applied to treating diseases associated with activated STAT proteins, particularly STAT3 activity, such as cell proliferative disorders, inflammatory reactions, and autoimmune conditions.



INTERNATIONAL SEARCH REPORT

International application No.

· · · · · · · · · · · · · · · · · · ·			PCT/US04/1206	0
A. CLA IPC(7)	SSIFICATION OF SUBJECT MATTER			
US CL	: A61K 38/00, 48/00 : 514/2,44			
According to	International Patent Classification (IPC) or to both n	ational class	sification and IPC	
B. FIEL	DS SEARCHED			
Minimum do	ocumentation searched (classification system followed	by classific	ation symbols)	
U.S. : 5	514/2,44			
Documentati	on searched other than minimum documentation to the	e extent that	such documents are included	in the fields searched
Electronic da STN: Medlin	ata base consulted during the international search (nan ne CAPlus US Patents Derwent	ne of data ba	ase and, where practicable, sea	arch terms used)
	UMENTS CONSIDERED TO BE RELEVANT			
Category *	Citation of document, with indication, where			Relevant to claim No.
X,P	ULANE, CM et al. STAT3 ubiquitylation and deg cytokine and oncogene signaling. Journal of Virolo 6385-6393.	radation of logy, June 20	Mumps virus suppress 03, Vol. 77, No. 1, pages	1-47
х	KUBOTA, T et al. Association of mumps Virus V protein with RACK1 results in			16-47
	dissociation of STAT-1 from the alpha interferon re	ceptor com	plex. Journal of Virology,	10-47
	December 2002, Vol. 76, No. 24, pages 12676-12682.			,
x	YUKOSAWA, N et al. C-terminal region of STAT-1alpha is not necessary fo its ubiquitination and degradation caused by mumps virus V protein. Journal of Virol December 2002, Vol. 76, No. 24, pages 12683-12690.		not necessary fo its n. Journal of Virology,	16-47
				-
	documents are listed in the continuation of Box C.	See patent family annex.		
Special categories of cited documents: "A" document defining the general state of the art which is not considered to be of particular relevance		"T"	later document published after the international filing date or priori date and not in conflict with the application but cited to understand principle or theory underlying the invention	
	plication or patent published on or after the international filing date	. "X"	document of particular relevance; the considered novel or cannot be considered when the document is taken alone	
"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)		-Y-	document of particular relevance; the considered to involve an inventive ste	p when the document is
"O" document referring to an oral disclosure, use, exhibition or other means		combined with one or more other such being obvious to a person skilled in the		
"P" document published prior to the international filing date but later than the priority date claimed		"&"	document member of the same patent	family
Date of the actual completion of the international search		Date of mailing of the international search report 08 DEC 2004		
01 November 2004 (01.11.2004) Name and mailing address of the ISA/US		Authorize		
Mail Stop PCT, Attn: ISA/US			7. 11.	+ 1 C. /
Commissioner for Patents P.O. Box 1450		Jon Eric Angell J. While		
Alexandria, Virginia 22313-1450 Facsimile No. (703) 305-3230			: No. 703-308-1235	For
		L		
Urm PC 1/15A	/210 (second sheet) (January 2004)			

INTERNATIONAL SEARCH REPORT

International application No.

PCT/US04/12066

Box No	Box No. I Nucleotide and/or amino acid sequence(s) (Continuation of item 1.b of the first sheet)				
1. With inver	regard to any nucleotide and/or amino acid sequence disclosed in the international application and necessary to the claimed nation, the international search was carried out on the basis of: type of material				
	a sequence listing				
	table(s) related to the sequence listing				
b.	format of material				
	in written format				
	in computer readable form				
c.	time of filing/furnishing				
	contained in the international application as filed				
	filed together with the international application in computer readable form				
	furnished subsequently to this Authority for the purposes of search				
2.	In addition, in the case that more than one version or copy of a sequence listing and/or table relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.				
3.	Additional comments:				
	\cdot				
•					